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Two types of foveation strategy in 'latent' nystagmus

Fixation, visual acuity and stability

L. F. Dell'Osso [1-3]
R. J. Leigh [1-4]
N. V. Sheth [1,3]
R. B. Daroff [1,2,4]

[1] Ocular Motor Neurophysiology Laboratory and [4] Neurology Service, Veterans Affairs Medical Center; and the Departments of [2] Neurology and [3] Biomedical Engineering, Case Western Reserve University and University Hospitals of Cleveland; Cleveland, OH, USA

Abstract The authors studied the foveation dynamics of two individuals with latent/manifest latent nystagmus (LMLN) to test the hypothesis that oscillopsia suppression and good visual acuity require periods of accurate target foveation at low slip velocities. Congenital nystagmus (CN) waveforms contain post-saccadic foveation periods; the LMLN waveform does not and yet allows for both oscillopsia suppression and good acuity. During fixation with both eyes open, there were intervals when the eyes were still and correctly aligned; at other times, there was esotropia and nystagmus with slow-phase velocities less than ±4 deg/sec and each fast phase pointed the fovea of the fixating eye at the target. However, cover of either eye produced LN and a different strategy was employed: the fast phases carried the fixating eye *past* the target and the fovea subsequently reacquired it during the slowest parts of the slow phases. The authors confirmed this in both subjects, whose high acuities were made possible by foveation occurring during the low-velocity portions of their slow phases. A nystagmus foveation function (NFF), originally developed for CN, was calculated for both LN and MLN intervals of fixation and it was found to track visual acuity less accurately for individuals with high acuity. Individuals with LMLN exhibit two different foveation strategies: during low-amplitude LMLN, the target is foveated immediately after the fast phases; and during high-amplitude LMLN, target foveation occurs towards the end of the slow phases. Therefore, the saccadic system can be used to *create* retinal error rather than eliminate it if this strategy is beneficial. Individuals with LMLN foveated targets with the same eye-position and -velocity accuracy as those with CN and the NFF provides a rough estimate of acuity in both. Current calibration methods for both infrared and search-coil techniques need to be altered for subjects with LMLN.

Correspondence and reprint requests to: L.F. Dell'Osso, Ph.D., Ocular Motor Neurophysiology Laboratory, Veterans Affairs Medical Center (127A), 10701 East Boulevard, Cleveland, OH 44106 USA,
Telephone: (216) 421-3224
Fax: (216) 844-3160
E-mail: lfd@po.cwru.edu

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Key words Latent/manifest nystagmus; visual acuity; oscillopsia

Introduction This paper mainly addresses where 'foveation' occurs during the latent/manifest latent nystagmus (LMLN) waveform. In normal subjects, who can maintain steady fixation of a small visual target, it is possible to determine the measured eye position that corresponds with foveation by assuming that the maintained eye position results in the target image being at the center of the fovea. In subjects with congenital nystagmus (CN), there is agreement that a similar estimation can be made provided well-developed 'foveation periods' occur and visual acuity is normal.

Individuals with CN point their foveae at an object of interest (foveation) to accurately maintain the image within the foveal area at low retinal slip velocities.[1] These periods of extended foveation occur after the *foveating* fast phases that are part of each cycle of most CN waveforms (pendular with foveating saccades, jerk, jerk with extended foveation, pseudopendular with foveating saccades, bidirectional jerk and dual jerk).[2] Periods of extended foveation occur after non-foveating *braking* saccades in pseudocycloid and pseudojerk waveforms.[3] There are no such post-fast-phase periods of extended foveation in pendular, asymmetric pendular, pseudopendular or triangular waveforms. Because of the periods of extended foveation in most CN waveforms, high visual acuities are possible.[4-11] Despite slow-phase velocities that can exceed 200°/sec, we and others hypothesized that the ability to accurately position the eyes on target in successive CN foveation periods was necessary for oscillopsia suppression.[1,11-17]

Another, different type of infantile nystagmus is LMLN, first described in 1872.[18] Later, the term, 'latent' was erroneously used to describe this nystagmus, thinking that it only appeared upon cover of one eye.[19] In 1947, Kestenbaum realized that this nystagmus also appeared with both eyes open and coined the oxymoron, 'manifested latent' nystagmus.[20] Our studies, and others,[21] suggest that the latter is the more common case. LMLN is a combination of these two terms since, as the name implies, LMLN is a singular entity with two stimulus conditions. Consistent with the original terms, when the nystagmus is present with one eye covered, we designate it as latent nystagmus (LN) and when present with both eyes open (but one in a tropic position due to strabismus with its vision cortically suppressed), as manifest latent nystagmus (MLN). LMLN differs from CN in: waveform (implying a different underlying mechanism); the necessity for accompanying strabismus;[22] and the nature of the variation with both gaze angle and fixating eye.[23] The LMLN slow phases are of decreasing velocity or, for low amplitudes, linear; those of CN are of increasing velocity or are pendular.

In the early 1970's the foveation of subjects with CN was studied by filming their retinas while they fixated a laser spot. The resulting films documented that CN waveforms caused the eyes to move away from and back to the target and not across it, as had been previously presumed.[24] While conducting this study, we had the opportunity to film a subject with LMLN. Analysis of that film (by LFD and RBD) showed that the low-amplitude and low-velocity LMLN slow phases of the subject caused the fixating eye to drift away from the laser spot and the fast phases refoveated it. Three of the authors of this paper (LFD, RJL and BFR) have reanalyzed that film and confirmed that original impression. Due to the nature of the LMLN slow phases, there are no post-saccadic periods of extended foveation. This has been hypothesized to be due to the high initial velocities or accelerations of linear and decreasing-velocity slow phases.[25] Yet, individuals with LMLN, as those with CN, may exhibit normal visual acuity and rarely complain of oscillopsia. If the same basic requirements for acuity and oscillopsia suppression exist in the two populations, how is this accomplished?

We investigated the foveation dynamics of an individual with LMLN who had normal acuity to determine how these feats were accomplished in the presence of the LMLN waveform. Upon determining the mechanisms used by this subject, we verified the findings in a second subject with LMLN and poorer visual acuity. Because retinal image velocity reduces visual acuity and motion perception and may cause oscillopsia, an understanding of the foveation dynamics in LMLN contributes to our understanding of these sensory processes.

Case histories

SUBJECT 1 The main subject of this study (S1) was a 36-year-old woman who had been referred with a ten-year history of headaches and occasional horizontal oscillopsia. She was diagnosed clinically as having CN, esotropia, rotary nystagmus and MLN. There was no family history of headache and she was not on oral contraceptives. A variety of symptomatic medications were not beneficial for what was diagnosed as tension-type headaches. Neurological examination uncovered no abnormalities except for her eye movements.

Ocular motility recordings on two occasions, separated by 18 months, confirmed that she had alternating esotropia and documented a combination of torsional and LMLN which were temporally unrelated to her headaches; she did not have CN. Horizontal saccades showed a torsional component. Her visual acuity was: 20/20−2 (OD); 20/20−2 (OS); and 20/15 −2 (OU). The monocular acuities were measured while the other eye was occluded. She had a dissociated vertical deviation and approximately 5D (prism diopters) of esotropia. Bagolini lenses positioned with only 5-10° misalignment (unlike the standard perpendicular orientation) create a striking stereo illusion in binocular individuals. This consists of a light streak seemingly emanating from the source and traveling toward the observer. When recognized, the illusion presumably reflects the presence of central and peripheral stereoscopic mechanisms. Testing this subject with such 'stereo' Bagolini lenses revealed rudimentary peripheral stereopsis.

SUBJECT 2 The second subject (S2) was a 10-year-old boy with strabismus and nystagmus, examined for the first time in our laboratory when he was four years old, one year after he had undergone a strabismus operation. His nystagmus was a mixture of intervals of LMLN and of CN, with the former predominant. The intervals of CN allowed accurate calibration of the eye movements. This was an important consideration in this study since it allowed verification of the calibration procedure used in S1. The nystagmus was mainly horizontal, with a pendular torsional component. In addition, he had occasional square-wave jerks, square-wave pulses[26] and some saccadic dysmetria; none of the latter interfered with either his acuity or our analysis of his nystagmus. He preferred fixating with his left eye in adduction (right gaze) while his right eye was esotropic. His visual acuity was: 20/70 (OD); 20/25 +1 (OS); and 20/20-1 (OU).

Methods

RECORDING Horizontal, vertical and torsional rotations of both eyes were recorded using the 'double loop' scleral search coil method with six-foot field coils (CNC Engineering, Seattle, WA). The coil system bandwidth was 0-150 Hz, linear range of greater than ±20° and sensitivity of 0.1° in all three planes. The subject's head remained within the 30 cm cube of the magnetic field where the translation artifact was less than 0.03°/cm. Data were filtered (bandwidth 0-90 Hz) and digitized at 200 Hz with 16-bit resolution using a DT2801/5716A Data Translation board. Coils (Skalar, Delft, The Netherlands) were calibrated using a protractor device capable of rotations in each plane. Although calibrated, coil data was adjusted for bias during analysis. The mean foveation position of each eye was set to 0° to align it to the target position during fixation in primary position. This is routinely done for most other types of eye-movement recording methods and although it does not guarantee that the 0° eye position coincides with a target image on the center of the fovea, it does place 0° at the subject's chosen point of fixation; except for rare cases of extrafoveal fixation or certain types of foveal aplasia, it is reasonable to equate 0° with the foveal center, especially when the subject has good vision. Horizontal and vertical rotations of the coils of up to 20° produced less than 0.5° of crosstalk in the torsional channel. Studying fixation in primary position eliminated the effects of either vertical or torsional eye displacement on the horizontal signal. Horizontal eye movement recordings were also made using infrared reflection. Eye positions and velocities (obtained by analog differentiation of the position channels) were displayed on a strip chart recording system (Beckman Type R612 Dynograph). The total system bandwidth (position and velocity) was 0-100 Hz. Infrared data were digitized at 200 Hz with 12-bit resolution using a DT2801 Data Translation board. Targets were 0.2° light-emitting diodes (LED).

PROTOCOL This research, involving human subjects, followed the Declaration of Helsinki and informed consent was obtained after the nature and possible consequences of the study were explained. The research was approved by an institutional human experimentation committee.

ANALYSIS Data analysis (and filtering, if required), statistical computation of means and standard deviations, and graphical presentation were performed on an IBM PS/2 Model 80 using the ASYST software for scientific computing. Further details on ASYST may be found elsewhere.[27]

To calculate the SD of the LMLN waveform's foveation periods in a given interval of fixation (*e.g.*, 10 seconds), the point of minimum eye velocity (minimum slope) in each slow phase was identified interactively on the position record and, using array mathematics, tested to ensure simultaneous satisfaction of both position (±0.5°) and velocity (±4°/sec) criteria. Thus, the epochs in which slow-phase velocity was minimal were identified and the SD of position calculated to measure if the eye was at a similar position during each epoch. To calculate the total time per second (or per cycle) that the target was truly foveated, the eye-position and eye-velocity arrays were analyzed (also using array mathematics) for all points when both the ±0.5° and ±4°/sec limits of the predefined 'foveation window' were satisfied.

We also used *phase plane* analysis to study the simultaneous relationship between the position and velocity of the eye (and, hence, of retinal image). The trajectories seen on phase plane plots are always in a *clockwise* direction if the conventions of rightward direction and velocity being positive are adhered to. Saccadic movements appear as high-velocity clockwise loops; rightward saccades would show positive velocities and directions while leftward saccades would be negative. The trajectories of respective slow movements would also appear clockwise, with lower velocities. During fixation, phase planes enable immediate identification of those periods when the target image is both stable and on the fovea. During smooth pursuit or vestibuloocular reflex (VOR) analysis, phase planes of retinal image motion or gaze identify those periods of stability indicative of good pursuit or VOR respectively. Further details on the use of phase planes may be found elsewhere.[1,16,28] *Scanpath* plots (vertical *vs.* horizontal motion) of both position and velocity allowed us to determine if the minima for eye position or velocity were synchronous in the horizontal and vertical planes. Unlike the classical scanpaths of normals during viewing of a complex scene, these are scanpaths of the eyes produced by ocular oscillations during fixation of a single target (*i.e.*, nystagmus scanpaths). These and the phase planes provided evidence of *simultaneous* satisfaction of the position and velocity criteria in both planes.

Results The eye movement data taken from S1 during two sessions separated by 18 months did not contain any significant differences in fixation or LMLN waveforms. Both sets of data contained intervals of no nystagmus and low-amplitude MLN during viewing with both eyes open and both contained high-amplitude LN upon occlusion of one eye.

OPHTHALMIC EXAMINATION In an attempt to duplicate the evaluation of the relationship between the waveform of LMLN and target foveation, we studied the fixation of S1 using an ophthalmoscope. With both eyes open, S1 was instructed to fixate the 'star' target projected by the ophthalmoscope while several of the authors independently determined whether the fast phases were taking the fovea towards or away from the target. The subject had a low-amplitude MLN during these tests. All concluded that the MLN slow phases took the center of the fovea of the fixating eye away from the target and the fast phases refoveated it.

EYE MOVEMENT DATA Based on our experience from the retinal movies and our ophthalmoscopic analysis of S1, we made the initial assumption that foveation occurred at the ends of the fast phases and defined 'zero' eye position as the mean of these positions. To facilitate analysis, we adjusted the position bias of the fixating eye in each record based on that assumption. During MLN, the fixating eye is always the eye given by the direction of the fast phase of the nystagmus, as is the case for LN where the other eye is occluded. Thus, during low-amplitude MLN (*i.e.*, binocular viewing), the right eye bias (in both the horizontal and vertical planes) was adjusted so that the ends of the rightward fast phases (post-dynamic overshoots, if present) took the right eye to the center of the target. Similarly for the left eye, the adjustment was made during left-eye fixation (jerk left MLN) with both eyes open. The same bias adjustment was applied to all respective eye-position records

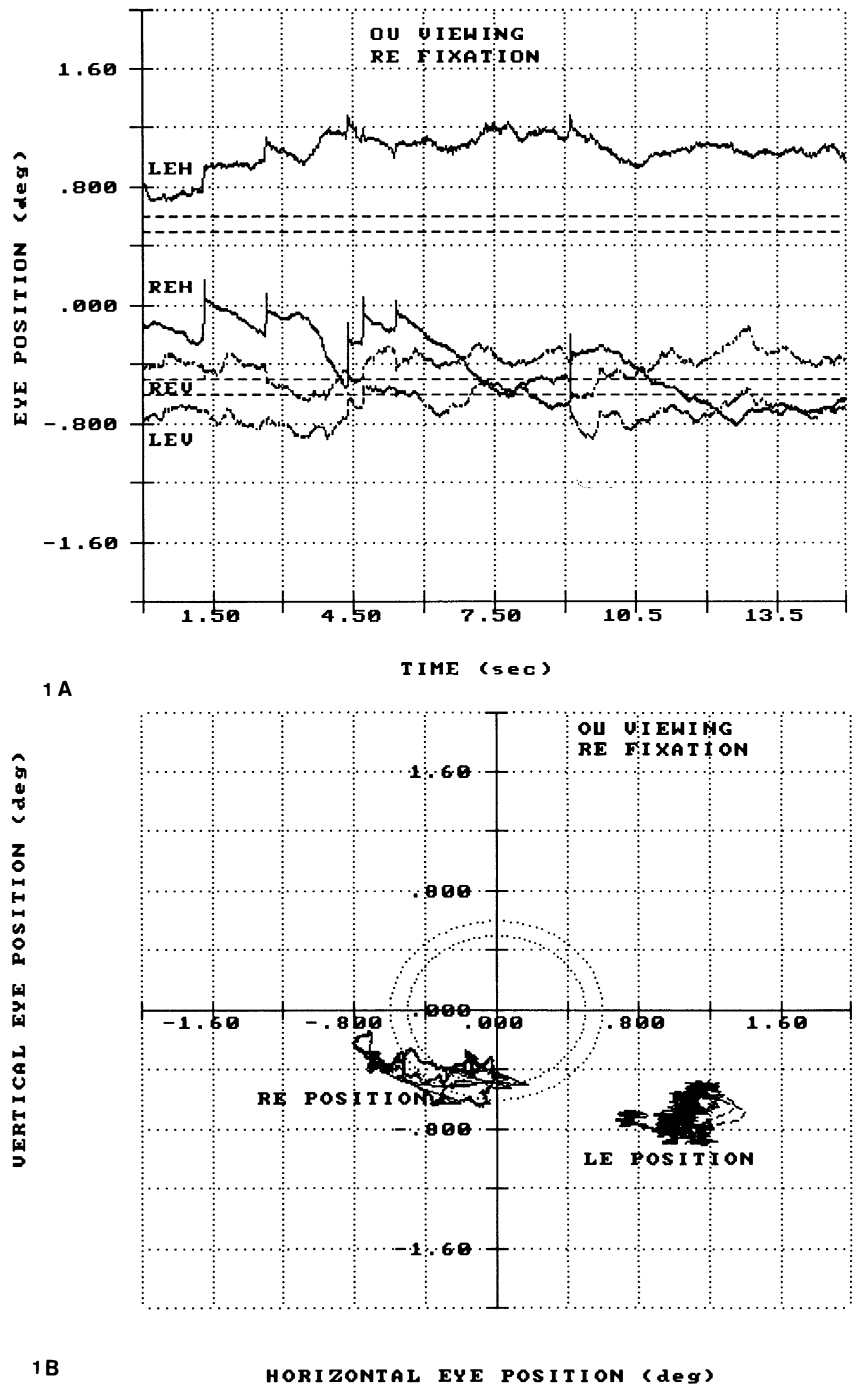
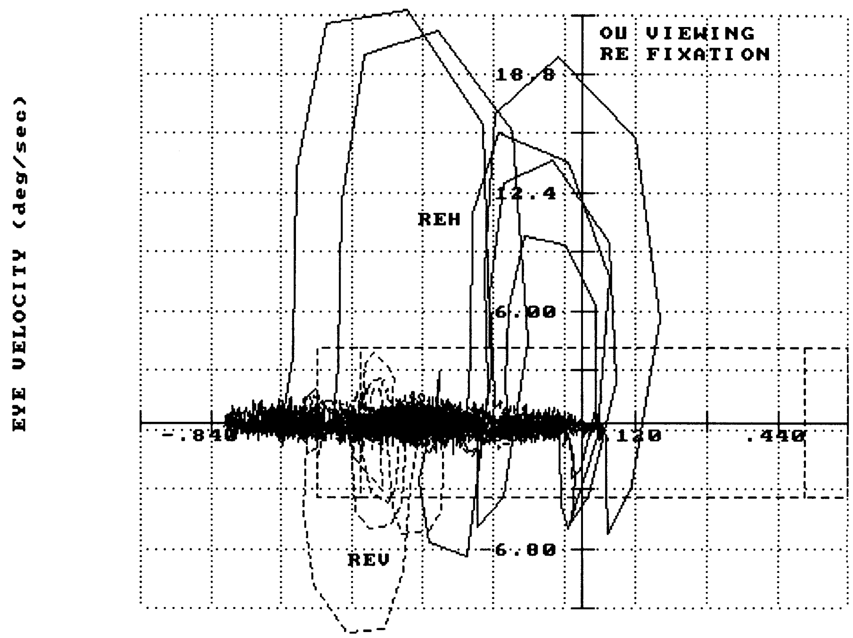


Fig. 1. Right and left eye data from Subject 1 during 15 seconds of right-eye fixation (jerk right MLN) while both eyes were viewing a 0.2° LED in primary position. (a) Horizontal and vertical position *vs.* time records. The left eye was esotropic and slightly hypotropic.(b) Position scanpaths of both eyes showing the fixating right eye on target and the tropic left eye.(c) Phase planes of the horizontal (solid) and vertical (dashed) trajectories of the fixating right eye. The large clockwise, high-rightward-velocity loops are the MLN fast phases; the clockwise, high-leftward-velocity loops show a small downward component to the MLN. All slow phases in both planes were well within the foveation window. In this and other figures: RE – right eye; LE – left eye; OU – both eyes; REH – right eye horizontal; LEH – left eye horizontal; REV – right eye vertical; LEV – left eye vertical. Dashed lines in time plots and scanpaths indicate the 0 ± 0.5° foveal extent and a 0.1° additional position allowance for the radius of the target. Dashed lines on phase planes indicate foveation windows (0 ±0.5° by 0 ±4°/sec) and a 0.1° additional position allowance for the radius of the target.

in each plane regardless of the occlusion condition.

The horizontal and vertical records shown in Fig. 1a illustrate right-eye fixation during jerk right MLN after the bias of the right-eye data was adjusted. The left-eye positions are shown biased by the value that was determined during an interval of left-eye fixation and jerk left MLN. Each eye's bias adjustment was determined during fixation by that eye while a low-amplitude MLN was present. Note the prominent dynamic overshoots in the fast phases of the fixating eye and the lack of absolute conjugacy of the strabismic left eye; the latter is a common observation for subjects with strabis-



1C

mus and either LMLN or CN. Our LMLN records show that the strabismic eye often moves less than the fixating eye, as though it were decoupled from the ocular motor signals driving the latter. From t=10 sec onward there is a 5-sec period with no LMLN and a 1° left-eye esotropia. This may reflect a lack of attention by the subject after 10 sec of fixation on an LED or intermittent peripheral fusion. We also recorded the torsional movements of both eyes in addition to the horizontal and vertical components. Despite a ±2° variation in torsion, no torsional oscillopsia was perceived; this tolerance has been also noted for normal subjects. Fig. 1b shows the position scanpaths of both eyes during this same 15-second epoch. The left eye is eso- and hypotropic. In Fig. 1c, the horizontal and vertical phase planes of the right eye reveal the foveating nature of the small rightward fast phases (clockwise, high-velocity loops in the horizontal trajectories) of the MLN and the low velocities of the slow phases. The fixating right eye is almost always within the foveation window defined by the ±0.5° by ±4°/sec dashed rectangle and the extension of ±0.1° representing the radius of the target. The latter was added to account for the uncertainty of the exact fixation point introduced by a target of known size; this uncertainty was minimized by choosing small targets for fixation studies.

We next investigated the initial (transient) effects, on both the nystagmus and eye position (*i.e.* strabismus), of occlusion and removal of occlusion in both eyes. Fig. 2a shows the eye position records of both eyes when the left eye was occluded and when the occlusion was removed. Initially, S1 was fixating with *both* eyes. This is indicated by the absence of either MLN or strabismus in either eye. We found that when both eyes were within the foveal area of ±0.5°, the MLN ceased. Upon occlusion, the left eye immediately began to assume an esophoric position simultaneous with the initiation of jerk right LN in both eyes. Note that, based on our initial assumption of right-eye position that corresponded to foveation during jerk right MLN, the

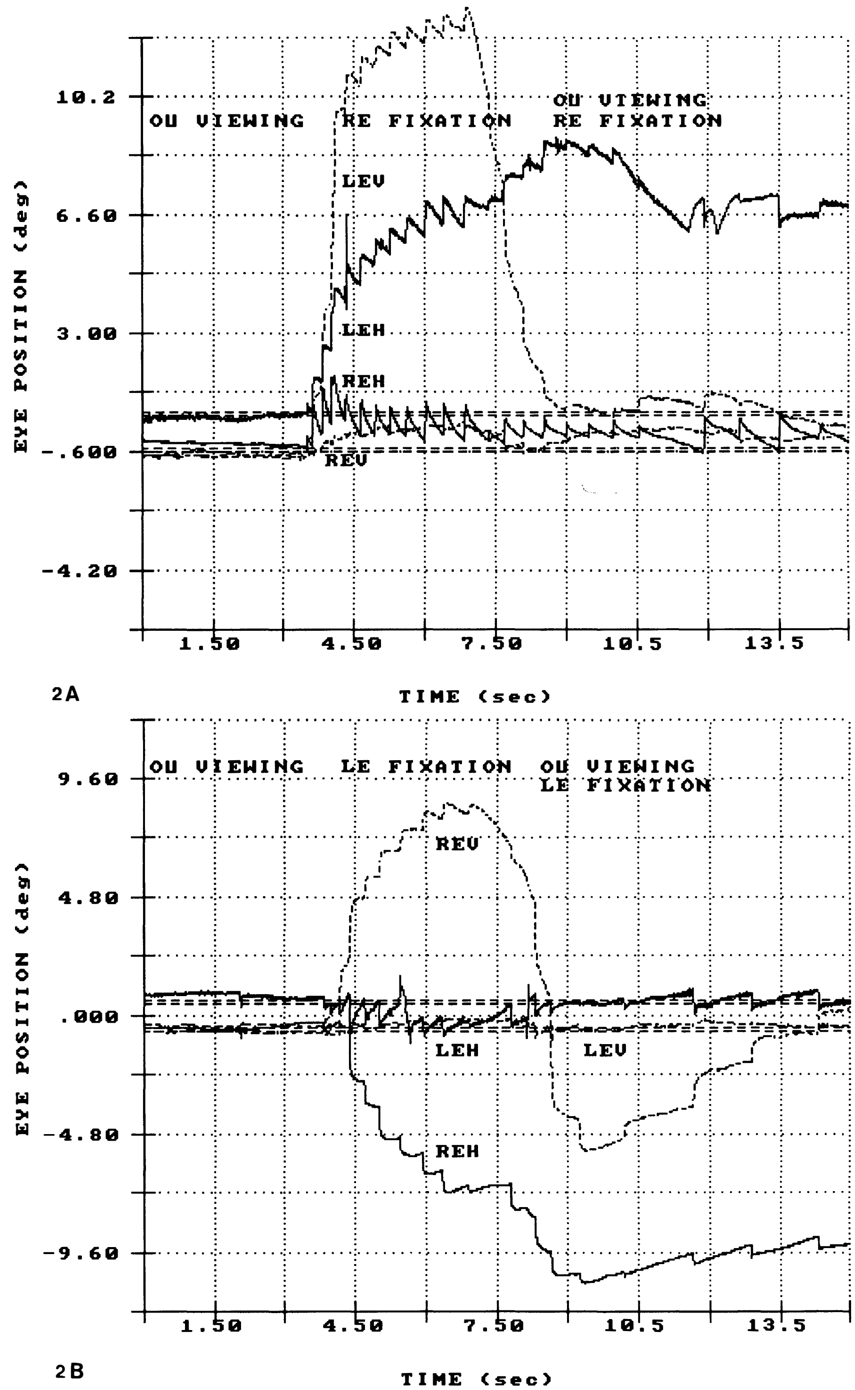


Fig. 2. Right and left eye data from Subject 1 showing the transient effects of occlusion in horizontal and vertical position *vs.* time records. (a) At the beginning of the record both eyes were open and fixating; there was neither nystagmus nor strabismus. At 4 sec, the left eye was covered (producing right-eye fixation with jerk right LN) and at 7 sec, cover was removed (converting the LN to MLN). (b) At the beginning of the record both eyes were open and fixating; there was neither nystagmus nor strabismus. At 4 sec, the right eye was covered (producing left-eye fixation with jerk left LN) and at 7.5 sec, cover was removed (converting the LN to MLN).

fast phases of the LN in the fixating right eye were then taking the center of the fovea *away* from the target, the opposite of their function during low-amplitude MLN (see Fig. 1a). When the occlusion of the left eye was removed (before the esophoric eye reached its final position), the right eye maintained fixation with a jerk right MLN while the esotropia of the left eye was reduced somewhat. Again, note the lack of conjugacy in the strabismic left eye, including what appear to be several disjunctive saccades at t = 12, 12.75 and 13.5 sec.

Fig. 2b illustrates the initial effects of transient occlusion of the right eye, allowing left-eye fixation. Again, at the beginning of the record *both* eyes were fixating; occlusion induced right-eye esophoria and jerk left LN, and removal of occlusion resulted in jerk left MLN. The lower amplitude of the LN in this case resulted in fewer fast phases taking the fixating left eye out of the foveation area than for the jerk right case. In both cases, the slow phases placed the fixating eye within this area.

We then made records of 15 seconds of fixation during occlusion of each eye to investigate the foveation dynamics during sustained LN in each direction when the nonfixating eye was in its steady-state phoric position. Fig. 3a

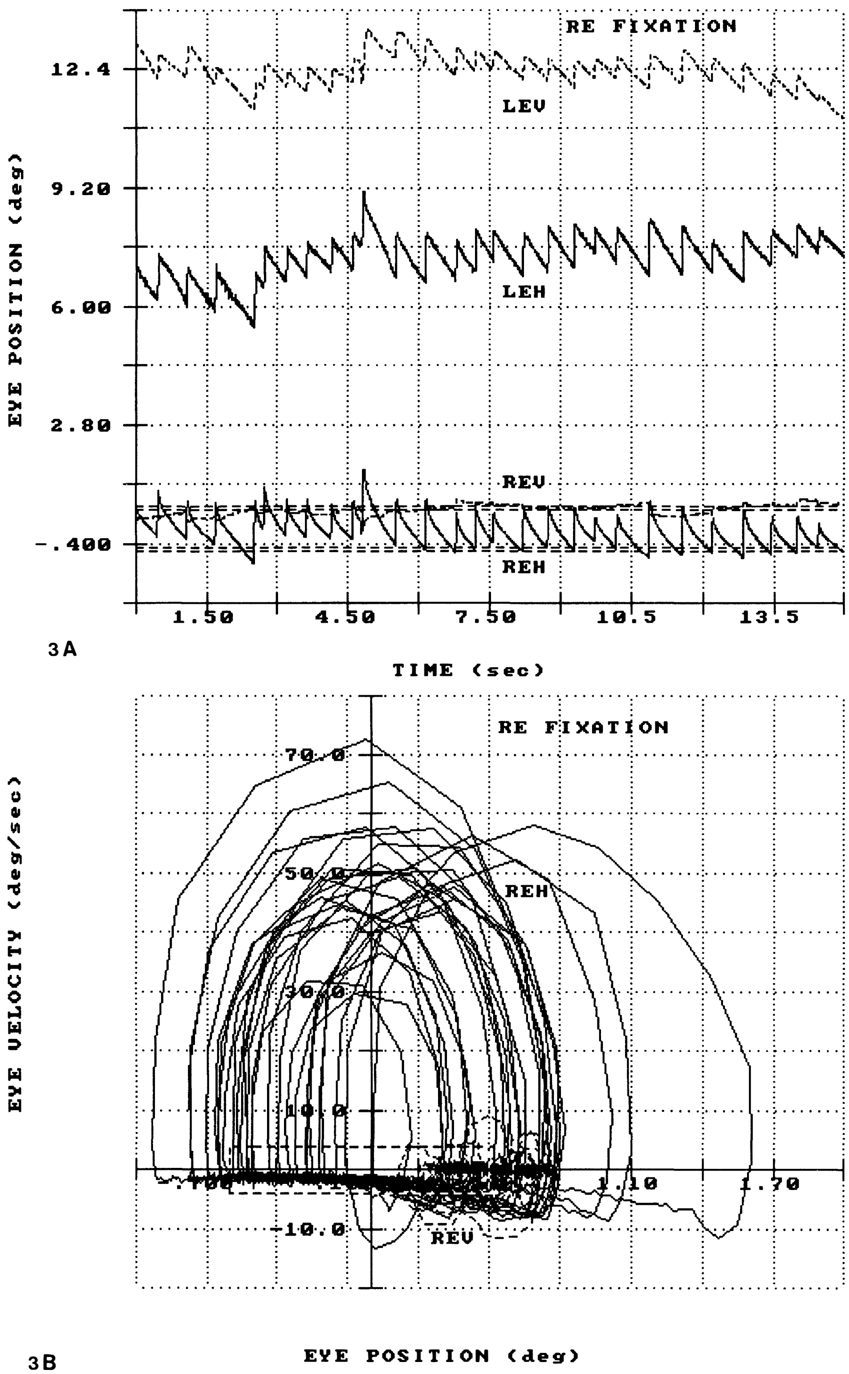


Fig. 3. Right and left eye data from Subject 1 during 15 seconds of left-eye occlusion (right-eye fixation). (a) Horizontal and vertical position *vs.* time records. The jerk right LN fast phases took the target image across the center of the fovea and sometimes outside of the foveal area while the decelerating leftward slow phases took it back into the foveal area. The left eye was both eso- and hypertropic. (b) Phase planes of the horizontal (solid) and vertical (dashed) trajectories of the fixating right eye. The clockwise, high-rightward-velocity loops are the fast phases of the jerk right LN and took the right eye to the right of the foveation window with leftward post-saccadic velocities that were outside of the foveation window; the decelerating leftward slow phases took the eye into the window.

shows a pronounced jerk right LN with the left eye in an esophoric position (≃ 7°). The fast phases brought the right eye out to the edge of the foveal area (dashed lines) or beyond and the decreasing velocity slow phases returned it. The covered left eye was in an eso- and hyperphoric position. Fig. 3b shows more dramatically that, although near the edge of the foveal area, the negative terminal velocities of the rightward fast phases (clockwise, high-rightward-velocity loops) were higher than the foveation window's boundary. In Fig. 4a, the fast phases of the jerk left LN were larger and took the foveating left eye farther from the target, again allowing the decelerating

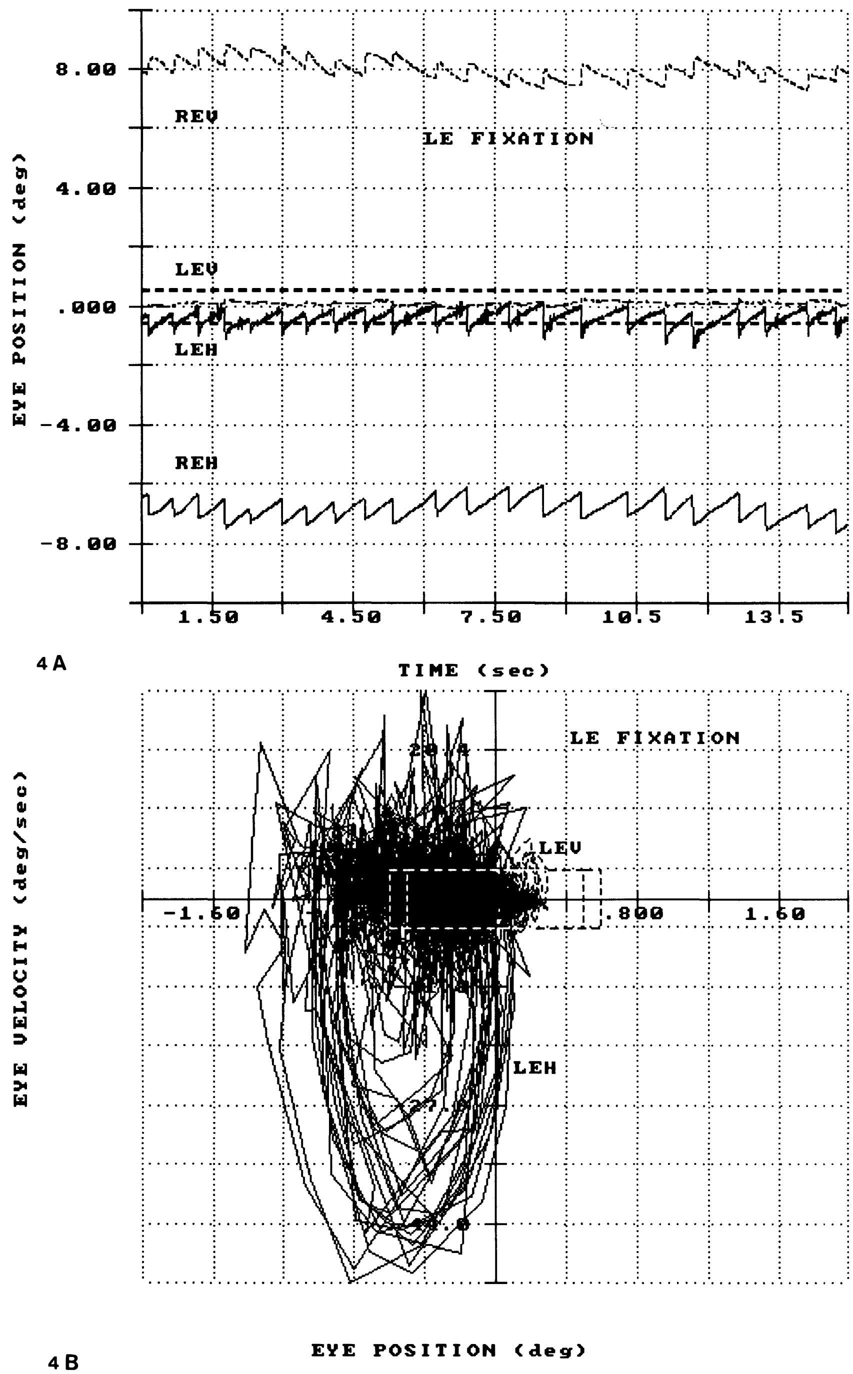


Fig. 4. Right and left eye data from Subject 1 during 15 seconds of right-eye occlusion (left-eye fixation) (a) Horizontal and vertical position *vs.* time records. The jerk left LN fast phases took the target image across the center of the fovea and usually outside of the foveal area while the decelerating rightward slow phases took it back into the foveal area. The right eye was both eso- and hypertropic. (b) Phase planes of the horizontal (solid) and vertical (dashed) trajectories of the fixating left eye. The clockwise, high-leftward-velocity loops are the fast phases of the jerk left LN and took the left eye to the left of the foveation window with rightward post-saccadic velocities that were outside of the foveation window; the decelerating rightward slow phases took the eye into the window.

rightward slow phases to refoveate the target. The covered right eye was in an eso- and hyperphoric position. As Fig. 4b shows, both the terminal leftward positions and rightward velocities of the leftward fast phases (clockwise, high-leftward-velocity loops) were outside of the extended foveation window. The target was foveated by the rightward, decreasing velocity slow phases.

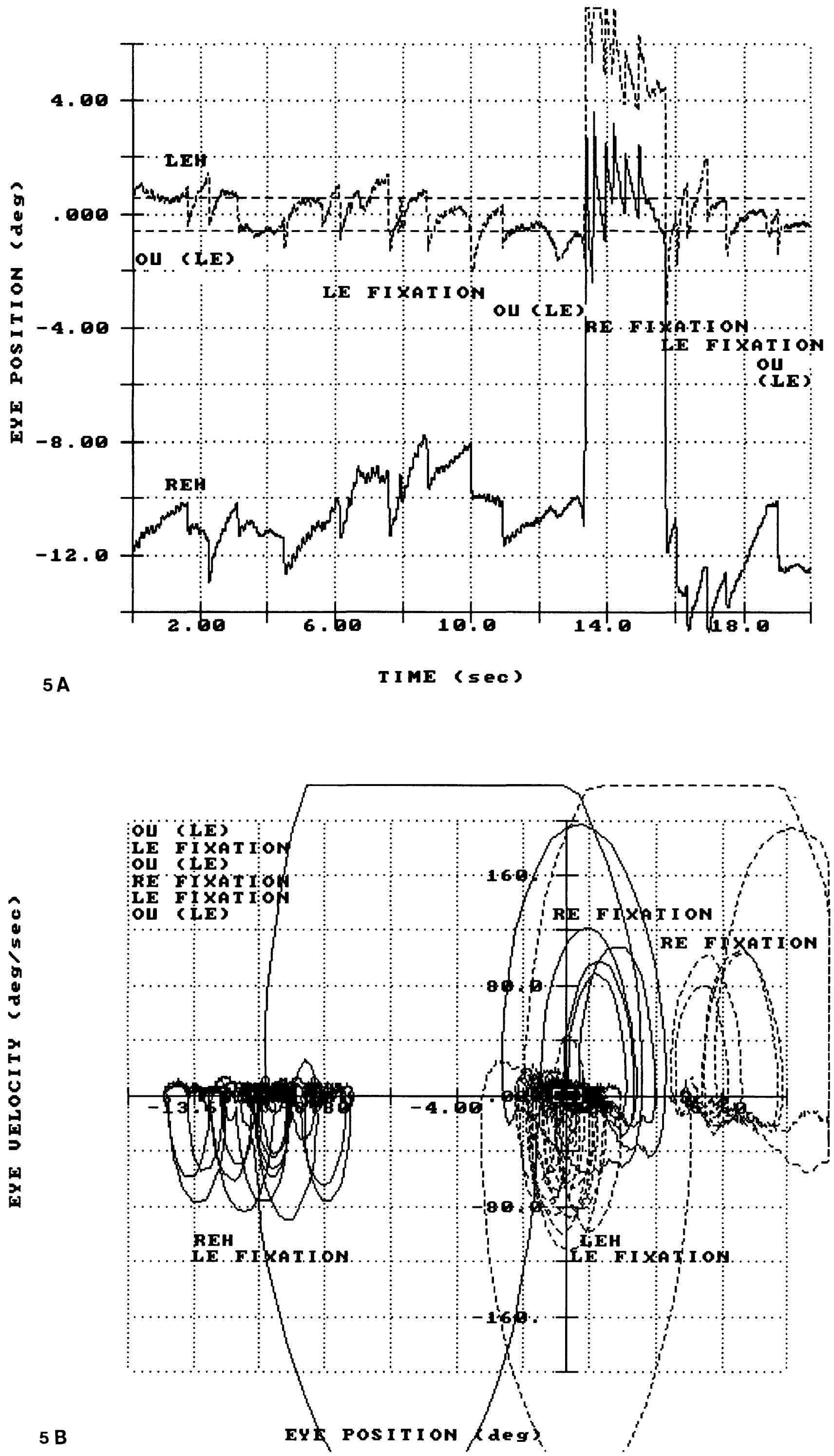
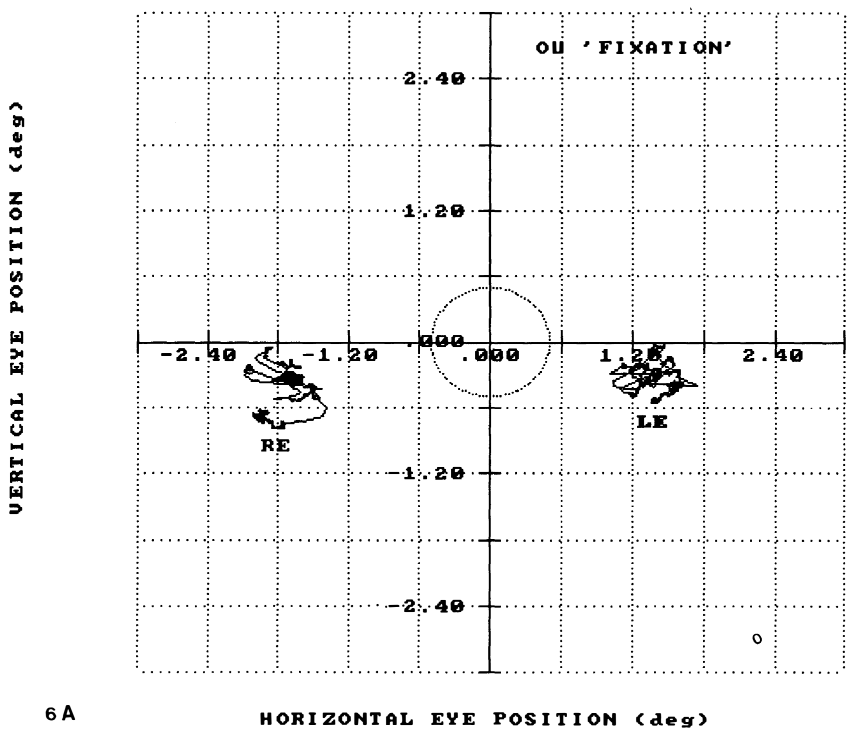


Fig. 5. Right (solid) and left (dashed) eye horizontal data from Subject 2 showing the effects of right and left-eye occlusion as well as reverse occlusion. In both (a) and (b), the fixating eye during binocular viewing is shown in parentheses. (a) Horizontal position *vs.* time records. At the beginning of the record both eyes were open with the left eye fixating and there was jerk left MLN. At 5 sec, the right eye was covered, converting the MLN to LN. At 11 sec, cover was removed, reestablishing jerk left MLN. At 13 sec, the left eye was covered, producing jerk right LN. At 15.5 sec cover was reversed, converting jerk right LN to jerk left LN. Finally, at 18 sec, cover was removed (converting the LN to MLN). The leftward and rightward fast phases took the respective fixating eye across the target and the ensuing slow phases refoveated the target. During all intervals of left-eye fixation, the right eye was esotropic; during the interval of right-eye fixation, the left eye was esotropic. (b) Phase planes of the horizontal trajectories of both the right (solid) and left (dashed) eyes during the viewing conditions described in (a). During left-eye fixation, the clockwise, high-leftward-velocity loops took the eye to the left of the foveation window with high rightward post-saccadic velocities. During right-eye fixation, the clockwise, high-rightward-velocity loops took the eye to the right of the foveation window with high leftward post-saccadic velocities.

Exactly the same methods of analysis and adjustment of the eye-position bias that we had developed for S1 were used for S2. Fig. 5a shows the horizontal position *vs.* time records of both eyes during several conditions of occlusion and fixation. Initially, both eyes were open and fixation was with the left eye (indicated by the jerk left MLN), with the right eye in an 8–12° esotropic position. At approximately 5.5 sec into the record, the right eye was occluded and a large (2°) jerk left LN ensued. Five fast phases took the left eye past the target. At approximately 11 sec, the occlusion was removed, reducing the nystagmus. At approximately 13.5 sec, the left eye was occluded and a large (2–3°) jerk right LN appeared during this interval of right-eye fixation; the left eye assumed an esophoric position of 4–8°. Five fast phases took the right eye past the target. At approximately 15.5 sec, cover was reversed to the right eye and the left immediately took up fixation (jerk left LN) while the right moved to a 12–14° esophoric position. Four fast phases took the left eye past the target. Finally, at approximately 18 sec, cover was removed and the previous jerk left LN became a lower amplitude jerk left MLN. Although S2's fixation was more variable than S1's, *defoveating* fast phases and foveation during the tail ends of the slow phases were evident for fixation of both eyes, whether during occlusion (LN) or with both eyes open (MLN). Fig. 5b shows the horizontal phase planes of both eyes for this record. During right-eye fixation, the fast phases (clockwise, high-rightward-velocity loops) of the right eye terminated to the right of the window with high leftward initial slow-phase velocities; the following leftward slow phases entered the window. The left eye is shown in its esophoric position. During left-eye fixation, the fast phases (clockwise, high-leftward-velocity loops) of the left eye terminated to the left of the window with high rightward initial slow-phase velocities; the following rightward slow phases entered the window. The right eye is shown in its esophoric position. Fig. 5 demonstrates that the same initial transient changes take place in the LMLN of this subject as did for the first subject (Figs. 2a and 2b).

To confirm our analysis and setting of the foveation positions of each eye, we reanalyzed the data from S1 using longstanding methods employed in our and others' laboratories. The bias of each eye was adjusted based on the assumption that, during LN (one eye occluded) the *fast phases* of the fixating eye foveated the target. Using those adjustments, the data taken during a ten-second record, of fixation with both eyes open, showed that *neither* eye ever foveated the target (see Fig. 6a). The left eye appeared to be 1.2–1.6° esotropic and 0.2–0.4° hypotropic during the record that included both a three-second interval of no nystagmus and a seven-second interval of right-eye fixation and jerk right MLN. Furthermore, the right eye appeared to be 1.4–2.0° esotropic and 0.2–0.8° hypotropic during these same intervals. This total absence of target foveation by *either* eye is incompatible with both S1's visual acuity of 20/15-2 OU and her lack of oscillopsia. Fig. 6b shows both eyes on target throughout the record when, in the absence of steady binocular fixation, the biases were adjusted based on the findings of this study using the position variability of the LMLN fast and slow phases.

THE NYSTAGMUS FOVEATION FUNCTION To better identify the position of the null region in CN, we developed a nystagmus foveation function (NFF) that would peak more sharply than nystagmus intensity.[1] This function also was noted to reflect visual acuity in the subject we studied. That is,



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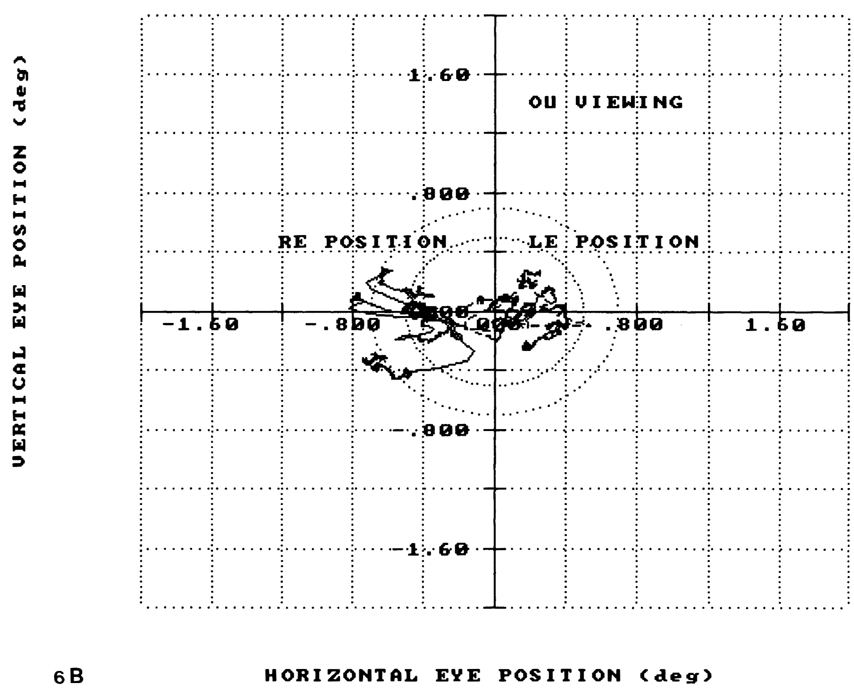

6B

Fig. 6. Position scanpaths of right and left eyes during ten seconds of fixation with both eyes open. (a) Bias adjustments made based on assumption that fast phases of LN foveate the target. (b) Bias adjustments made based on observation that low-amplitude MLN fast phases foveate the target but not high-amplitude LN or MLN. Outer dashed lines indicate allowance for the 0.2° radius of the fixation point used for this record.

higher values of NFF, measured under different gaze-angle and convergence conditions, correlated with the visual acuities measured under those conditions. We calculated the NFF for both S1 and S2 during each viewing/fixation condition. Table 1 summarizes the NFF calculations, the foveation times and the visual acuities corresponding to each fixation condition; also shown for comparison, are the values for the CN subject originally studied. S2 preferred left-eye fixation, since his right eye was amblyopic. The measured acuity (OU) reflects the higher acuity of the left eye. Thus, for both

TABLE 1. Nystagmus foveation function.
NFF = (TF * f) / (SDp * SDv)
TF – Foveation time per cycle
TFOV – Foveation time/sec.
f – nystagmus frequency
SDp – Standard deviation of mean foveation position
SDv – Standard deviation of mean foveation velocity.

Fixation <Nystagmus>	*NFF (sec/deg2)*	*TFOV/sec*	*VA*
<LMLN>			
S1			
'OU' RE	19.62	0.95	20/15-2
'OU' LE	2.73	0.59	20/15-2
RE	4.23	0.72	20/20-2
LE	1.92	0.54	20/20-2
S2			
'OU' RE	0.46	0.29	
'OU' LE	1.71	0.76	20/20-1
RE	0.37	0.20	20/70
LE	0.89-1.41	0.51 – 0.75	20/25+1
<CN>			
OU	0.73	0.34	20/25
OU	0.39	0.17	20/40

CN and LMLN, the NFF provides some indication of visual acuity. More precisely, in the absence of sensory defects that might limit acuity, the NFF measures the negative effect of the nystagmus (CN or LMLN) on the best possible acuity of an individual.

Discussion We have presented evidence to show that, although the foveation strategies exhibited during LMLN may differ from those during CN, the same criteria are met. To achieve high visual acuity, targets must be foveated during the low-velocity tail end of the LMLN slow phases and the suppression of oscillopsia is accomplished by accurately foveating the target on each successive cycle of LMLN. These findings affect both current models of ocular motor control and calibration of individuals with nystagmus.

Determination of the position of the fovea in relation to the target during LMLN, required a subject (S1) who could accurately use the center of the fovea. S1, who had a visual acuity of 20/15 OU, satisfied this criterion. Furthermore, since she was capable of intervals of binocular fixation with no nystagmus and did not experience oscillopsia during our testing, we were assured that she was accurately positioning her fovea on a *cycle-to-cycle* basis.[14,15] The intervals of low-amplitude MLN in her recordings, allowed adjustment of the bias of each eye's position data with minimal error. She also exhibited intervals of no MLN which presumably coincided with ocular alignment of the two eyes on target. These latter intervals would provide a further test of the bias adjustments of each eye. If they were correctly made, based on the alignment of each eye during fixation with low-amplitude MLN, then both eyes should be positioned within the foveal area (±0.5°) during the intervals when no MLN was present, as demonstrated in Figs. 2a and 2b.

To test the generality of our findings to others with LMLN and lower visual acuity, we studied the next subject with LMLN who was referred to our laboratory, without regard for visual acuity or purity of LMLN waveform. In this second subject, despite the presence of CN waveforms and occasional saccadic intrusions, target foveation during the LMLN waveforms was identical to that of S1. Since S2 was capable of intervals of CN with foveation periods, we were able to verify our calibration using the CN foveation periods. Furthermore, we retrospectively examined many of the approximately 100 records we have of LMLN subjects. Our examinations of previous data included subjects with either LMLN alone, or intervals of either CN or LMLN. In the former, eye-movement calibration had been carried out during monocular occlusion based on the assumption of LN fast-phase foveation. In the latter, calibration was correctly carried out during CN intervals using the foveation periods of the CN waveforms. Looked at retrospectively, with our current understanding of the foveation dynamics of LMLN, the data were more easily interpreted and provided a sound basis for the good acuity and lack of oscillopsia in such subjects. That is, there was greater eye-position variability at the ends of the fast phases than at the ends of the slow phases.

THE UNDERLYING MECHANISMS OF FIXATION IN LMLN The fixation records of S1 further demonstrate the necessity for strabismus in the genesis of LMLN.[22] Whenever both eyes were within ±0.5° of the target, there was no nystagmus (Figs. 2a and 2b). The eyes did not have to be exactly aligned with both target images at the centers of the foveae to suppress the LMLN. When one eye moved to a tropic position, either MLN (both eyes open) or LN (one eye occluded) developed. We and Abadi have hypothesized that the drift of both eyes in the nasal direction (with respect to the fixating eye) was due to an inability to switch between monocular and binocular afferent information.[29,30] The relative roles of the magnitudes of the visual signals and the calculation of egocentric direction are unclear but both seem to be involved in the determination of the resulting slow-phase, drift velocity.

Our data suggest that two distinct strategies for target foveation are employed by subjects with LMLN. (1) If the LMLN is of low amplitude with low-velocity, (usually) linear slow phases, the target is foveated by the fast phases and the fixating eye then drifts slowly away from it. Due to the low slow-phase velocity, the target image remains within the foveation window and acuity is not adversely affected. (2) If, however, the LMLN is of high amplitude with high-initial-velocity decreasing-velocity slow phases, the fast phases take the fixating eye past the target and it then drifts with decelerating velocity towards the target. The fast phases may take the target image out of, or to the edge of, the ± 0.5° foveal area and the slow phases return it towards, or through, the foveal center. Thus, variability is tolerated as long as the low-velocity portions of the slow phases bring the target image somewhere within the foveal area. Again, since retinal slip velocity is low during the intervals when the target image is within the foveal area, visual acuity is maximized. In many subjects, the MLN is of low amplitude and occlusion induces a higher amplitude LN.

As the phase planes demonstrate, the fixation strategies used in LMLN, although different from those of CN, accomplish the same result. They allow for a period of target foveation at low retinal slip velocity for each cycle (allowing high visual acuity) and do so repeatably from cycle to cycle (preventing oscillopsia).

PRIOR DATA REVISITED WITH 20/20 HINDSIGHT Previous data in the literature contain position biases due to the practice of calibrating each fixating eye by assuming that LN fast phases always foveated the target. The magnitude of these errors in eye position depend on the amplitude of the LN that was recorded; it could be fractions of a degree or several degrees. Given the results of this study, it should be possible to more accurately interpret eye movements of subjects with LMLN[22,31] or combinations of LMLN and CN.[23,32,33] For those with CN waveforms alone, we can accurately calibrate eye position using the foveation periods of the waveform. Data from subjects with the nystagmus blockage syndrome (type 2), where the initial CN waveforms convert to MLN with purposive esotropia, provide a unique condition where the calibration may be correct if performed while the waveforms were only those of CN (*i.e.*, there was no esotropia); the same applies for those with both LMLN and CN. In the blockage syndrome, the onset of the purposive esotropia would be reflected accurately in the records of both eyes. The position of the fixating eye can then be compared during normal distance viewing (CN waveform) and during distance viewing with purposive esotropia (MLN waveform). Fig. 2 of a previous study of the blockage syndrome shows one such record.[32] At the beginning of the figure, both eyes were on target (15° in right gaze) and the CN waveform was jerk right with extended foveation. The target was foveated during these periods of extended foveation. As the right eye moved to an esotropic position, the fixating left eye converted to a jerk left MLN waveform. As the recording shows, it was the tail ends of the MLN slow phases that moved the fixating eye to the same position as the CN periods of extended foveation that preceded this interval of esotropia; the leftward fast phases took the eye away from that position. That is, target foveation took place during the slow, tail ends of the MLN slow phases and not during the post-saccadic periods following the fast phases. At the end of the record, when both eyes were fixating, the jerk right with extended foveation CN waveform returned. The two successive periods of extended foveation show a leftward, binocular drift of fixation position.

Another type of subject where calibration is accurate and LMLN can be evaluated is one whose predominant waveform is CN (used for calibration) with an LMLN waveform appearing upon cover of one eye. In one such subject whom we studied, the CN waveforms eventually converted to a dual jerk latent waveform 3 sec after cover of the left eye. Initially, with both eyes open, the waveforms were CN with the left eye fixating and the right in an esotropic position. Upon cover of the left eye, it assumed an esotropic position and the right eye took up fixation with small, pendular CN. This evolved into a dual jerk right latent waveform induced by a leftward drift and in which the rightward fast phases took the right eye away from or through the target, creating retinal errors.

We have recorded the eye movements of approximately 100 subjects with LMLN. Several of these had sporadic occurrences of what resembled an LMLN waveform, with decreasing-velocity slow phases and fast phases towards the fixating eye. Between these intrusions on fixation, the eyes were still, sometimes for several seconds. Such data created some confusion regarding both the individual diagnoses and our conception of LMLN (*i.e.*, could the fast phases be the initial, defoveating movement?). At the time, we were under the impression that our retinal cinematography, which had identified the first foveation strategy, precluded such an interpretation of LMLN. Therefore, these subjects were thought to have saccadic pulses intruding on their fixation instead of, or in addition to, LMLN. Recently, we have re-evaluated these records and conclude that they did indeed represent LMLN whose fast phases were taking the fixating eye *away* from the target. However, LMLN is *not* a fast-phase instability, as we had speculated, but is a true nystagmus (being driven by the slow phase) that may cause the subject to respond to higher drift rates by deliberately making saccades (fast phases) past the target. This is in contrast to saccadic pulses, a type of saccadic intrusion, where stable fixation is interrupted by a saccadic pulse followed by its exponential drift back to target. In retrospect, target foveation during low-velocity portions of LMLN should not be surprising since those with LMLN can have good acuity and do not complain of oscillopsia. A recent study of normals who can voluntarily move their eyes in both planes ('roll' their eyes) showed that oscillopsia accompanied such movements unless the movements were separated by approximately 80-msec periods of relative eye stability.[34] This is the first evidence that such 'foveation periods' are required by normals as well as those with CN or LMLN and suggests that efference copy alone, although used by the ocular motor system, is insufficient to suppress oscillopsia.

OCULAR MOTOR SYSTEM IMPLICATIONS OF SACCADIC DEFOVEATION

The newly discovered second strategy exhibited by subjects with LMLN to achieve target foveation at low retinal slip velocities is one of repeatedly making saccades (fast phases) that take the eye *past* the target. Our models of the saccadic system are based on repositioning the eye to *reduce* retinal positional error to zero, not to *create* such an error. The models are predicated on a simple response to a target position input. This basic mode of operation now appears to be subject to alteration thereby serving higher functions, such as achieving better visual acuity and suppressing oscillopsia. Incorporation of such influences into ocular motor models should expand their usefulness in predicting responses to more complex stimuli under differing mental or attentional states.

The initial drifts of LMLN appear to be linear, suggesting a response to a tonic, directional imbalance (similar to the vestibular imbalance that produces vestibular nystagmus). At some point, when this drift exceeds a velocity threshold, the subject changes the way in which the saccadic system is used. For low-amplitude LMLN, normal foveating saccades are generated; in some individuals, these saccades contain dynamic overshoots. For high-amplitude LMLN however, two changes appear to occur: *defoveating* saccades are generated and the neural integrator is inhibited from integrating the pulse of activity responsible for generating these saccades. Such control of the neural integrator has been postulated before, in subjects with gaze-evoked nystagmus[35] and in the abducting saccadic pulses of internuclear ophthalmoplegia.[30,36] The results of this latter strategy are saccadic pulses that transiently take the eyes away from the target and are followed by decreasing-velocity drifts back to the target. Since the high-velocity drifts responsible for this type of LMLN are presumably still present, we hypothesize that the subject's fixation mechanism acts to slow them as the target image enters the foveal area and allow foveation with low retinal slip.

EXTENSION OF THE NYSTAGMUS FOVEATION FUNCTION The NFF was developed to allow a more positive identification of the CN null region. It is important in evaluating CN and possible therapies, to relate waveform changes to possible improvement in acuity; measuring acuity directly often introduces a large inter-subject variability due to anxiety effects causing increased nystagmus and may mask improvements in acuity that would be appreciated by the subject under normal viewing conditions. We observed that higher NFF's corresponded to higher visual acuities.[1] The NFF peaks sharply as foveation time rises and the accuracy of foveation (position and velocity) increases. As Table 1 shows, eventually additional changes in these variables cannot further improve acuity. A plot of an individual's acuity *vs.* NFF shows a saturation for higher values of NFF, as the acuity reaches the 20/20 to 20/15 range (as is indicated by the values in the table for both S1 and S2). For example, the NFF reflected the lower acuity in the amblyopic right eye (compared to the left) of S2. As NFF increases to values over 1.0, it is no longer a sensitive indicator of acuity and large changes in NFF will not reflect increased acuity. Below that value, the NFF tracks visual acuity across subjects for *both* CN and LMLN. That is, despite the differences in waveforms (reflecting underlying mechanisms) and variability with gaze angle, the NFF appears to include the relevant variables determining visual acuity. We are currently developing a function that will relate these nystagmus waveform characteristics to visual acuity more closely.

IMPLICATIONS FOR CALIBRATING INDIVIDUALS WITH LMLN The currently accepted methods of calibrating the eye-movement recordings of individuals with LMLN were derived from those developed for CN, where each eye is calibrated while fixating (the other being occluded) and, for IR methods, both the zero position and gain are adjusted using the foveation periods of each CN cycle. For search coil methods, only the zero-position bias need be adjusted since the gain of each coil can be set prior to the recording by using a protractor device. This methodology accurately positions and calibrates each eye independently and allows accurate measurement of the amount of strabismus throughout the recording session. In LMLN, it was thought that the fast phases *always* foveated the target, regardless of the amplitude of the nystagmus or of the shape of the slow phases. Therefore, in the same manner as for CN, each eye-position record was adjusted while that eye was fixating (the other being occluded) and exhibiting LN. As this study shows, there is a second foveation strategy that is employed during higher amplitude LN or MLN. When using this second strategy, fast phases take the fixating eye past the target allowing foveation during the latter part of the slow phases.

Given two foveation strategies, a different, and more difficult, calibration method is required. If there is no MLN present during calibration (an extremely rare condition), both eye-position records may be adjusted as they are for normal subjects. If the LMLN is of low amplitude with linear slow phases, each fixating eye-position record should still be adjusted so that the fast phases foveate the target both at zero and at the calibration angles to each side of primary (the latter for IR methods). The fixating eye is determined by the direction of either the MLN (when both eyes are open) or the LN (when one eye is occluded).

However, if the amplitude of the LMLN increases and the slow phases are of decreasing velocity, the fixating eye-position record should be adjusted to reflect target foveation at the low-velocity tail end of the slow phases. This includes both the zero and gain adjustments for IR, or the zero adjustment for search coil methods.

Since some preliminary findings from this paper were first presented at both NANOS and ARVO in 1993, they have been independently verified in two laboratories using scanning laser ophthalmoscopes (SLO). Richard Abadi (personal communication from Michael Gresty, who saw Dr. Abadi's SLO video) and Heinz Herbst of Tübingen (who showed an SLO video to one of the authors, LFD) produced SLO videos of subjects with LMLN. These videos clearly demonstrated that the fast phases brought the fovea past the target and the decelerating slow phases returned it.

In summary, we have identified a second foveation strategy employed by individuals with LMLN that complements the strategy previously documented by retinal cinematography. Both allow the same criteria for good acuity and oscillopsia suppression to be met as are met in CN. Accurate calibration of eye movement data requires recognition of these strategies.

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